INFORMATION

Greater St. Louis Citizens' **COMMITTEE FOR NUCLEAR INFORMATION**

ST. LOUIS, MISSOURI JANUARY 23, 1959

How Many Mice Make an Experiment?

An experiment with strontium 90 in mice which was widely publicized last fall concluded that strontium 90 from fallout "is extremely unlikely to induce even one bone tumor or one case of leukemia." Was this conclusion justified? A report on the experiment and the scientific controversy it provoked.

The answer to this strange question has become the subject of scientific debate after the conclusions of an article entitled "Mice, Men and Fallout" were given wide publicity last fall. The article *(Science, September 19, 1958)* was written by Dr. Miriam P. Finkel of Argonne National Laboratory. It presents the results of an experiment in which strontium 90 was injected into mice, and draws conclusions as to whether humans are in danger from strontium 90 in fallout.

Letters from scientists citicizing this experiment and its conclusions have recently appeared (*Science* December 19, 1958).

In Dr. Finkel's study, mice were given a single dose of strontium 90. They were then watched to see how long they lived and how many cases of bone cancer or leukemia developed. The mice were divided into 12 groups and each group received a different dose of strontium 90, ranging from low to high amounts. There were 150 mice in the group which received the lowest dose; other groups were smaller in size. At the lowest dose each mouse got 0.13 microcuries of strontium 90, an amount roughly equivalent to 70 times the value that is now considered safe for an adult man.

Results from Treated Mice

The results from the treated animals were then compared with a control group of 150 mice that had received no strontium 90.

- Mice given strontium 90 developed more bone cancer than those receiving none. The high doses resulted in many animals with bone cancer. Only 6 animals developed bone cancer at the lowest dose. (Three of the control mice also died of bone cancer.)
- In mice given low doses, cancers were found more often than in the control group, but the difference was not big enough to be statistically significant. The lowest dose that resulted in a significantly higher number of bone cancers in the treated animals was 20 microcuries of strontium 90.
- Mice given strontium 90 did not live as long as the control mice. The lowest dose that resulted in a statistically significant decrease in life span was about 4.4 microcuries – a value which corresponds to about 250 times the level set as permissible for humans.

The article concludes with an estimate of the danger to people from strontium 90 in fallout. Dr. Finkel interprets her experimental results with mice as evidence for a threshold – or safe level – for man that lies between 5 and 15 microcuries of strontium 90. (This value is 50 to 150 times as large as the present permissible level set by the ICRP – International Committee for Radiological Protection.) On this basis the researcher concludes with this final sentence, "In any case, the present contamination with strontium 90 from fallout is so very much lower than any of these levels that *it is extremely unlikely to induce even one bone tumor or one case of leukemia.*" (italics added)

Conclusion Not Certain

Although Dr. Finkel makesthis statement, her paper includes remarks which would tend to qualify such a conclusion. For example, commenting on the number of bone cancers seen at the lowest doses, she states, "... the threshold may actually lie below the latter dose. There were not enough animals at these levels to permit statistical verification of differences as small as those observed." In regard to another result on decreased life span, she calculated that a difference as small as that noted at the lowest dose would be reliably proven if it had been based upon about 9 times more mice than she used.

This qualification points to the key question regarding Dr. Finkel's data. If the expected number of bone cancers or premature deaths is a small fraction of the total number, a large number of mice must be used to see if the effect of radiation damage is really present. If too few mice are used in such a study, so that there are no statistically reliable effects at low doses, then how can one be sure about the safe or threshold level? Dr. Finkel felt justified in reaching her conclusions in spite of this problem, but other scientists are not willing to do so. (See below)

Is There a Safe or Threshold Level?

Whether or not there exists a safe level of strontium 90 is a question that scientists have been trying to answer for some time. The presence of a threshold means that the strontium 90 level in the population could increase up to a certain point without an increase in bone cancer or leukemia cases. As long as one stays below the threshold, one is safe; in exceeding it for a lifetime, the risk of bone cancer and leukemia is increased.

(Continued on back page)

First Data on Genetic Damage to Humans from Radiation

Two scientists study children of survivors of Hiroshima and Nagasaki and find evidence of a small but definite change in the sex-ratio as would be expected if radiation had caused heritable changes.

The effect of radiation on future generations is one of the questions with which scientists have been concerned, particularly since the world's population has been increasingly exposed to radioactive fallout.

Experiments have been conducted with microorganisms, insects and mice: in every organism tested ionizing radiations have been found to produce inherited changes – or mutations – in the offspring.

Since the composition and basic structure of the hereditary material is believed to be the same in man as in other organisms, there is every reason to expect a similar effect in human beings. But to determine this with certainty and to discover how many mutations are produced by a given dose of radiation in man are difficult problems. They require the comparison of children of non-irradiated parents with those of irradiated parents to learn whether the rate of mutations rises and if so how much.

J. W. Shull and J. V. Neel have made such a study (*Science*, August 15, 1958) by analyzing the sex-ratio of the children of survivors of the Hiroshima and Nagasaki bombings.

The Normal Sex-Ratio

The hereditary material is found in the cell nucleus in the form of thread-like chromosomes; most human cells contain 23 pairs. One of these pairs, which is made up of two kinds of chromosomes called X and Y, is responsible for determining sex. The body cells of women all contain a pair of X chromosomes; the body cells of men contain one X and one Y chromosome. When the female's eggs are produced the paired X chromosomes separate, each egg receiving a single X chromosome. When the male's sperm cells are formed the XY pair separates with half the sperm receiving an X and half a Y chromosome.

In this way the eggs have equal chances of being fertilized by a sperm cell carrying an X or Y chromosome. The result is that normally half of the offspring are girls (XX) and half boys (XY). Anything that affects this statistical balance will show up as a change in the ratio of boys and girls that are born.

How Radiation Can Change the Sex-Ratio

Shull and Neel reasoned that, as the atom bomb explosions over Hiroshima and Nagasaki exposed the population to radiation, some of this radiation would be expected to hit egg and sperm-forming cells, damaging one or more of the chromosomes inside by causing mutations. A great proportion of such newly-formed mutations would be expected, on the basis of what is known from experimental work on animals, to be so harmful as to be lethal, that is, to cause the death of the fertilized egg in which they occur. For this reason most new mutations are never observed. However, those lethal mutations which happen to affect an X chromosome can be discovered indirectly because they may result in a noticeable change in the ratio of boys and girls that are born.

Theory of how this takes place (see diagram): If women are irradiated, some of their X chromosomes may receive lethal mutations. Some of these mutations will be recessive; that is, they will kill the fertilized egg only in the absence of a normal X chromosome. If an egg carrying an X chromosome with a recessive lethal mutation is fertilized by a sperm carrying a normal X, the normal X suppresses the effect of the mutation and the fertilized egg develops into a girl. But if the same mutated X chromosome is in an egg that is fertilized by a Y-carrying sperm, the mutation has no normal counterpart contributed by the sperm and the fertilized egg dies. This egg (XY) would have produced a boy had it survived; so the effect of the mutation is to reduce the number of boys that are born.

By similar reasoning it is expected that the children of irradiated fathers and non-irradiated mothers will show a lowered percentage of females.

Results of Study

With the theoretical expectations just described, Shull and Neel compared the ratio of boys to girls among the offspring of Hiroshima and Nagasaki survivors. They organized their data into groups in which the father only, the mother only, or both parents were irradiated. Each group was then divided into 4 subgroups on the basis of the amount of radiation received.

In 10 of the 12 subgroups the change in the sex-ratio is in the direction required by the theory outlined here. That is, the irradiation of mothers tended to decrease the proportion of males, while the irradiation of fathers tended to increase it.

The changes indicated were so small, however, that a reliable estimate of the effect of a given dose of radiation on the sex-ratio cannot be derived from their data. The "best guess" would be that the proportion of males decreases by .006 following 100 rep of maternal radiation.
(rep: a measure of radiation energy absorbed by the body)

This work provides the first data consistent with the view that ionizing radiation causes mutations in man.

REMINDER ABOUT BABY TEETH

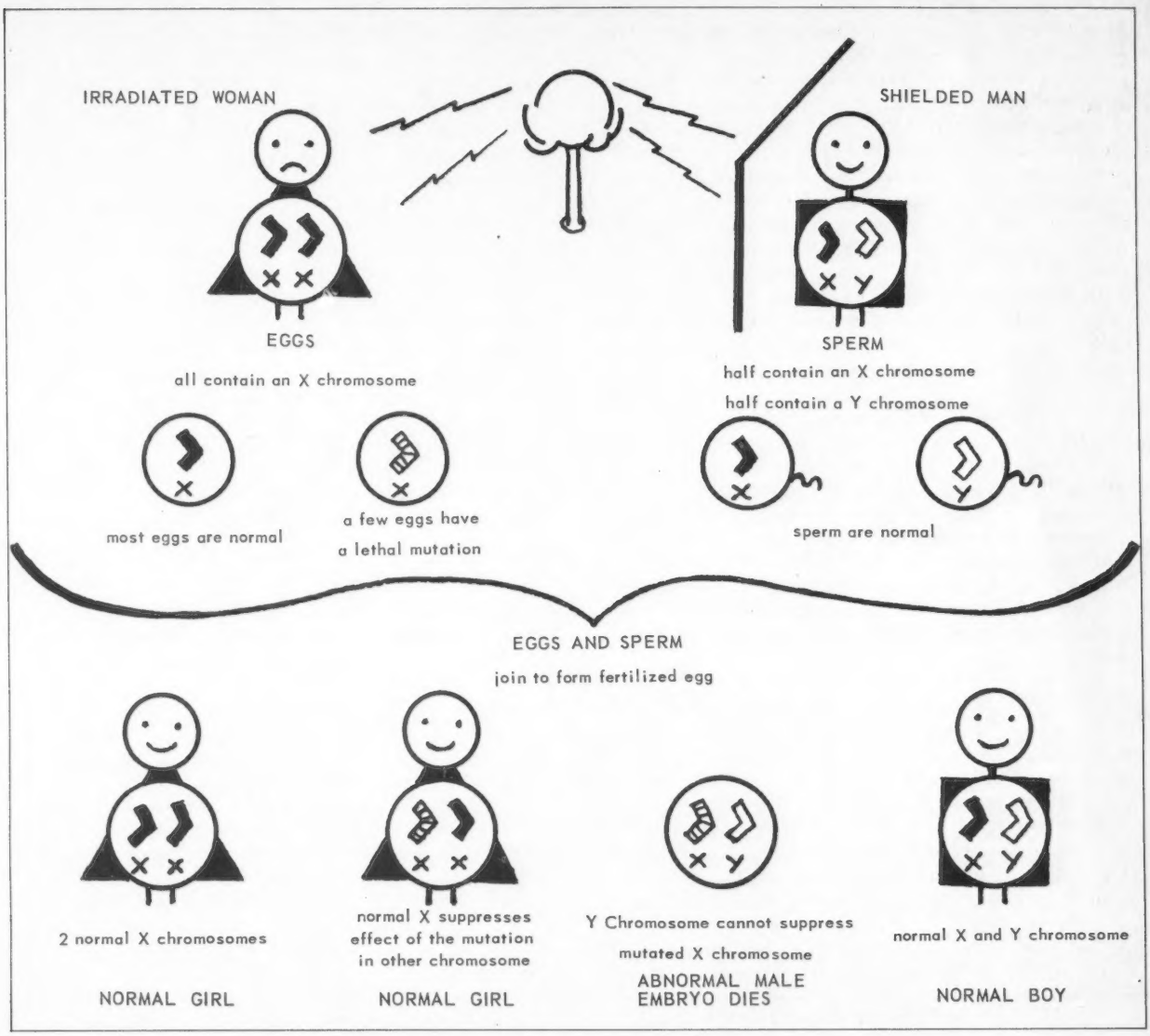
You can help scientists learn how strontium 90 accumulates in the human body by sending children's shed baby teeth to:

BABY TOOTH SURVEY
4484 West Pine Blvd.
St. Louis 8, Missouri

Forms showing the information about mother and child that should accompany each tooth are now available in quantity. Write or phone the office – JEfferson 3-0353.

HOW ATOM BOMB RADIATION AFFECTS THE BOY-GIRL RATIO

Example showing why there will be more girls than boys among children of irradiated mothers and non-irradiated fathers.



New Fallout Particles Reported to United Nations

Fallout particles of unusually large size and high radioactivity have been found in Sweden and Brazil, according to a New York *Times* article of January 12, 1959.

Discovery of the particles in Sweden was reported to the United Nations by Dr. Rolf M. Sievert, professor of Radiophysics at the Royal Caroline Institute of Stockholm. They resulted from Soviet nuclear blasts in the Arctic last fall, and were found 700 or more miles from the explosion site, as located by seismic observations in Sweden.

Dr. Sievert, quoted in the *Times*, said Swedish scientists had recently found particles " of very high individual radioactivity" in "short-lived fission products and radioactive material from local or tropospheric fallout."

"These particles produce doses that in a few hours are capable of causing total destruction of cells remaining in direct contact with them," he said. "The possible biological effects of such particles is a problem of great interest involving new aspects of the fallout problem."

The United Nations Scientific Committee on the Effects of Atomic Radiation, of which Dr. Sievert is a member, will study this report at its next meeting in March. It also has before it an earlier report from Dr. Bernard Gross and other nuclear physicists on the faculty of Catholic University in Rio de Janeiro which revealed that on June 25, 1957 "a single fallout particle of exceptional dimensions and activity" was detected by an observation post making a routine check of air pollution. This particle was thought to have originated from a British test in the South Pacific 7,900 miles away.

HOW MANY MICE MAKE AN EXPERIMENT? *(Continued from front page)*

The current approach to the possible danger from fallout by the authorities responsible for setting radiation safety levels (ICRP) utilizes the idea of a threshold level. This group has set the safe level of strontium 90 for the general population at 0.1 microcuries per adult.

Counter to the threshold idea is the notion that every bit of radiation absorbed by the body, even very small doses, carries with it a certain increase in the risk of damage. The best evidence for this is found in the field of genetics (study of inheritance) where animal experiments have demonstrated that genetic damage (number of mutations) depends upon the amount of radiation absorbed by the sex cells even at very small doses. There is only suggestive evidence at present that the same is true for bone cancer and leukemia. (These are called somatic effects as distinguished from genetic effects.)

Threshold Controversy Continues

Information about the threshold controversy is helpful in understanding why scientists have expressed certain divergent opinions on the danger of fallout. Calculations based on a threshold for leukemia or bone cancer would in general lead to estimates minimizing the danger. Those based on the absence of a threshold would emphasize the danger. Conclusive proof of the existence or non-existence of a threshold for somatic damage from radiation is not available, and therein lies the scientific rub. Which idea is correct?

The United Nations Scientific Committee on the Effects of Atomic Radiation could not find the evidence conclusively in favor of either idea in its Report issued last June. Two estimates were made for leukemia. One, assuming no threshold, predicts that continuation of nuclear tests would result in 60,000 new cases of leukemia each year; the other estimates that no increase in leukemia would result from continued testing if there is a threshold at 400 rem. (A rem is a unit of measure of radioactivity; 400 rem is about 20 times the threshold value for strontium 90 for the general population.)

That this controversy has not been laid to rest by Dr. Finkel's paper can be seen from the recent comment in *Science* by Dr. J. S. Roth of Hahnemann Medical College.

"At the lowest level of radiation used . . . the number of animals used should have been approximately 200,000 instead of 150 . . . Even with 200,000 animals it might be expected that only one mouse would develop a tumor as the aftermath of the radiation, and therefore the number utilized should be many times greater than 200,000 to establish a statistical significance of the effect at low levels. In view of this I think the final sentence in the conclusion is extremely unwarranted and is not in accord with an objective scientific appraisal of the data presented."

Dr. Carl Moos of the University of Illinois College of Medicine also objects to Dr. Finkel's conclusions in the light of the small number of mice used in the study:

"No. . .demonstration that there is a threshold different from zero seems possible from the data as presented. In fact, these data appear to indicate that the experimental design used is inadequate for this purpose . . . Unfounded statements *minimizing* radiation hazards can be especially harmful if they turn out later to have been false."

Geneticists Object

Objection from another point of view was made in a letter from two widely-known geneticists, Prof. L.C. Dunn and Prof. T. Dobzhansky, both of Columbia University. Dr. Dobzhansky was a member of the U.S. team of experts that participated in the preparation of the U.N. report on radiation. They criticize Dr. Finkel for reaching sweeping conclusions about fallout without considering the problem of damage to inheritance by radiation.

The scientific skirmish that is described here is of public interest because it illustrates the magnitude of the experiments that have to be done to get useful information about the biological effects of small doses of radiation. It is essential for the public at large to know about the importance and large financial cost of the studies that need to be done, so that widespread support for their undertaking will materialize.

Hunt for Radium Poisoning Cases

A search for persons exposed to radium 25 to 40 years ago is now under way at the Radioactivity Center at Massachusetts Institute of Technology. Persons sought are those who painted luminous watch dials with paint containing radium in the watch factories of the eastern seaboard and the Chicago area during the 1920's and 30's. Also sought are patients who received injections of radium salts or who drank radium water.

The purpose of the search is to study human beings with some 30 years exposure to radiation from radium in their bones to determine indirectly the long-term effects of strontium 90 from nuclear bomb fallout.

The current maximum permissible concentrations (MPC) of strontium 90 in bone are based entirely on the permissible levels of radium. (See "Radioactivity in St. Louis Milk," *Information,* CNI, November 24, 1958.) At present the MPC for radium is based upon a previous short-term study of only 78 cases of radium poisoning.

Serious questions regarding the safety of the radium MPC have been raised by Dr. W. Looney, authority on radium poisoning. He re-considered the radium dial painter cases and concluded that the radium MPC might have to be lowered. (*Science,* March 21, 1958.)

INFORMATION is published 10 times a year by the Greater St. Louis Citizens' COMMITTEE FOR NUCLEAR INFORMATION. Address: 4484 West Pine Blvd., St. Louis 8, Missouri. Telephone: JEfferson 3-0353 (9a.m. to 12 noon)

Editors of this issue: Virginia Brodine, Gloria Commoner. Contributors and consultants: Drs. Walter C. Bauer, H. T. Blumenthal, Hampton L. Carson, Barry Commoner, Irwin H. Herskowitz, Dale Kaiser, Harrison D. Stalker.

The Committee for Nuclear Information is an organization devoted to the gathering and public distribution of facts about the effects of nuclear war, nuclear testing, and non-military uses of nuclear energy.